

B1 NB-1, Lane 21: MASS-NB-SCH-1, Lane 22: negative control (sterile distilled water), Lane 23: molecular weight marker (same as Lane 2)).

Page 6, beginning at line 19, through page 7, ending at line 17, replace the paragraph with:

B2 Fig. 6 is a pair of photographs of electrophoresis of PCR products for NB-1 and MASS-NB-SCH-1 genomic DNA using primers designed based on PAC clone data. The gel used was 2.5 agarose. (Lane 1: marker (1202 bp, 517 bp, 396 bp, 201 bp), Lane 2: positive control (human placenta DNA), Lane 3: normal cells derived from neuroblastoma patient without 1p36 deletion, Lane 4: tumor cells derived from neuroblastoma patient without 1p36 deletion, Lane 5: normal cells derived from MASS-NB-SCH-1 patient, Lane 6: MASS-NB-SCH-1, Lane 7: NB1, Lane 8: positive control (mouse hybridoma with human chromosome), Lane 9: positive control (human lymphocytes), Lane 10: positive control (human placenta DNA), Lane 11: normal cells derived from neuroblastoma patient without 1p36 deletion, Lane 12: tumor cells derived from neuroblastoma patient without 1p36 deletion, Lane 13: normal cells derived from MASS-NB-SCH-1 patient, Lane 14: MASS-NB-SCH-1, Lane 15: NB1, Lane 16: positive control (mouse hybridoma with human chromosome), Lane 17: positive control (human lymphocytes), Lane 18: empty lane). In A, dJ1028013-SP6 was used as primer for Lanes 1-8; dJ142A6-T7 was used as primer for Lanes 9-17. In B, dJ371E1-SP6 was used as primer for Lanes 1-8; dJ587c9-SP6 was used as primer for Lanes 9-17.

Page 8, beginning at line 21, through page 9, ending at line 15, replace the paragraph with:

B3 Identification of the tumor suppressor gene is possible by analysis of Loss of Heterozygosity (hereunder also abbreviated as LOH). The chromosomes of human cells, except for the sex chromosomes, exist as pairs, and two copies of each gene are present, one from the mother and one from the father. According to the "two-hit theory" advocated by Kundson A.G. et al. (Kundson A.G., *Pediatr. Res.*, 10:513- (1976)), inactivation of a gene is only found to occur

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when both of each copy from the mother and father are inactivated, and LOH is observed most often by this mechanism. LOH refers to a pattern whereby a small genetic abnormality (deletion or substitution of a base or part of the gene) exists in one copy, while the chromosome on which the other copy resides undergoes the entire deletion of a large region including the gene. Consequently, in patients experiencing onset of cancer due to inactivation of a tumor suppressor gene, it is thought that there are two copies of the chromosome on which the tumor suppressor gene resides in normal cells, and one copy in tumor cells.

Page 14, beginning at line 15, replace the paragraph with:

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Two of the obtained confluent culturing plates were used to obtain cells by trypsin treatment. The obtained cells were suspended in 5 ml of TEN buffer (TEN: 50 mM Tris-Cl (pH 8.0), 1 mM EDTA, 100 mM NaCl) and homogenized. To the homogenized suspension there were added 750µl of SDS (10%) and 125µl of Proteinase K (MERCK Co., 20 mg/ml), and the mixture was gently mixed by inversion and incubated overnight at 50°C for lysis of the cells.

Page 15, beginning at line 8, replace the paragraph with:

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Next, 10.2 ml of ethanol which had been precooled at -20°C was added to and mixed with the collected supernatant, the resulting filamentous DNA was collected with a Pasteur pipette, the excess ethanol was removed and the DNA was dried. An appropriate amount of TE buffer (Tris-Cl (pH 8.0), 1 mM EDTA) was added to the dried DNA, and mixing was effected at room temperature for 1-2 days to dissolve the DNA.

(Example 2) Purification of genomic DNA extracted from human neuroblastoma cell lines.